Refer to: Khajawall AM, Sramek JJ Jr, Simpson GM: 'Loads' alert (Information). West J Med 1982 Aug; 137:166-168

'Loads' Alert

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"Loads," a combination of glutethimide and codeine, are a relatively new form of drug abuse that is increasing in popularity in the Los Angeles area as a heroin-substitute. Preliminary findings based on interviews and treatment of a group of preferential Loads abusers seen over a one-year period suggest that this combination has a potential for serious intoxications and withdrawal complications. The common withdrawal symptoms include those produced by both a sedative-hypnotic and a major narcotic and necessitate a detoxification plan based on the pharmacologic rationale of the abused combination.

IN THE WORLD of drug abuse there are many fads whose popularity and longevity depend on complex interactions between biosocial and economic factors. When the availability and quality of heroin are poor (and invariably the cost expensive), the drug culture experiments with various combinations to produce a comparable "high."[1-5] Currently in the Chicago area, the heroin-substitute is "T's and blues" (Talwin [pentazocine] and Pyribenzamine Hydrochloride [tripelennamine]).[4] In Los Angeles and surrounding areas it is "Loads" (glutethimide and codeine phosphate).[5] One Loads contains two tablets of glutethimide (totaling 1 gram) and four tablets of codeine No. 4 (240 mg); the latter are typically Empirin No. 4 (aspirin, 325 mg, and codeine, 60 mg) or Tylenol No. 4 (acetaminophen, 300 mg, and codeine, 60 mg). Although a dosage variant of this combination was reported over a decade ago,[1] there is little information available on the characteristics, treatment or potential complications of this relatively new drug combination.

The present investigation was undertaken at the Metropolitan State Hospital Drug Abuse Program (Norwalk, California), a major inpatient state-operated drug abuse, detoxification, evaluation and rehabilitation program servicing the Los Angeles metropolitan adult population. The drug detoxification service is used primarily by heroin-dependent patients. During the two years before this investigation we had admitted fewer than ten patients to this service who had claimed a Loads habit. However, over the past 12 months we have admitted 89 patients seeking detoxification from Loads (see Table 1). The following are the demographic characteristics of these patients: men, 60 percent and women, 40 percent; mean age, 27 years (range, 19 to 42); caucasians 80 percent, hispanics 16 percent and blacks 4 percent. For comparison, our typical heroin patient is 30 years of age, the male-to-female ratio is 3:1 and race is primarily hispanic, followed by caucasians and blacks. Of the 89 Loads patients, 65 were interviewed extensively to determine characteristics of Loads abuse; that is, prior favorite drug habit, withdrawal history (if previously attempted without medical supervision) and withdrawal symptoms, and significant problems encountered while taking Loads (accidents, and so forth).

Loads are ingested orally to produce an intoxication that is claimed to be an equivalent or better

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Submitted, revised, February 3, 1982.

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TABLE 1.—*"Loads" Admissions From November 1980 Through October 1981*

	11/80	12/80	1/81	2/81	3/81	4/81	5/81	6/81	7/81	8/81	9/81	10/81	Total
Number opiate admissions	93	104	136	110	154	129	142	138	106	81	74	82	1249
Number other* admissions	11	2	13	16	13	13	11	16	20	16	33	28	213
Number "Loads" admissions	1	3	4	3	5	6	5	5	15	7	12	23	89
"Loads" as percent of all admissions	1.0	2.7	2.6	2.3	2.8	4.1	3.2	3.1	10.6	7.2	10.1	17.3	5.7

*Phencyclidine hydrochloride (PCP), amphetamine, phenobarbital, cocaine or LSD.

ABBREVIATION USED IN TEXT

APC = aspirin, phenacetin and caffeine

"high" than that obtained with heroin. Most of our patients previously used heroin, but gradually shifted to Loads. Although the typical intravenous "rush" (or sudden onset) is absent, it can be approximated when Loads are taken on an empty stomach. Our patients reported that the intoxication is achieved within 20 minutes after ingestion, with the peak effect occurring after 40 minutes. Concurrent ingestion with ethanol reportedly intensifies this rush, suggesting an increase in the rate of drug absorption. The Loads-intoxicated state resembles that produced by ethanol and barbiturates and is characterized by alternating states of dream-like euphoria and "nodding." The latter term is commonly used in the drug culture to describe the somnolent part of this experience and is related to the soporific and stupefying effects of the drugs. Nodding is at times associated with brief or prolonged sensorimotor disturbances in the extremities and many of our Loads subjects had either experienced or presented with such disturbances.

In the beginning of this habit, the intoxication high reportedly persists for an average of 12 hours but increasing tolerance reduces it to three hours. In one patient, tolerance resulted in a habit requiring up to 12 Loads ingestions a day. These amounts are much higher than those previously reported[2,3] so that the potential for serious intoxications and difficult withdrawals is obvious. Most patients took one Loads daily at the start of the habit and were ingesting over three Loads just before detoxification. They gave a mean time interval of 24 hours between the last Loads ingestion and the beginning of withdrawal symptoms. Many of these patients had tried to withdraw from Loads themselves on a previous occasion, but apparently none were successful. Many of our patients encountered significant problems while taking Loads, such as coma, convulsions, peripheral neuropathies and major accidents, including automobile crashes, cuts and burns.

The persons under investigation also reported substitutions in the event of temporary unavailability of glutethimide or codeine: generally, another sedative-hypnotic for glutethimide, and another narcotic analgesic for codeine. The codeine is invariably taken as Empirin No. 4, Tylenol No. 4 or Tabloid APC (aspirin [227 mg], phenacetin [162 mg] and caffeine [32 mg]) with codeine No. 4 (60 mg). However, these substitute combinations are claimed to be less attractive than Loads. Some people stated that combining diazepam (Valium), 10 mg, with Loads expanded the peak period of the high and decreased the number of Loads needed to achieve the desired euphoric effect. Most people, however, categorically denied combining Loads with anything else, having known or heard about others who have died when mixing Loads with alcohol or other drugs. In Southern California, Loads were responsible for at least seven deaths during the first five months of 1981 (Los Angeles *Times,* August 14, 1981, p 19).

The commonly observed withdrawal symptoms include anxiety, sweating, severe headache, palpitations, insomnia, fever, abdominal pain, muscle spasms, diarrhea, vomiting, rhinorrhea, tremors, involuntary jerking movements of the limbs and convulsions. To provide a safe detoxification and prevent withdrawal reactions, we adopted two treatment regimens based on the pharmacology of this drug combination. After establishing the accuracy, duration, dosage and other aspects of the habit, we convert glutethimide and codeine doses to equivalent amounts of phenobarbital and methadone hydrochloride (500 mg of glutethimide

equals 60 mg of phenobarbital; 120 mg of codeine equals 10 mg of methadone). From a third to the full dose equivalent of converted glutethimide to phenobarbital is given for the first two to three days until a patient is drug free, after which the patient is observed carefully for another three days. The amount of phenobarbital given depends on the severity of the addiction and the presence of withdrawal symptoms. Methadone is given in a third of the dosage conversion on a twice-a-day decreasing scale over the first five to seven days of treatment.

Some variations in the above schedule are made depending on the total daily quantity abused and the duration of the habit. In general we have used a 15-day withdrawal schedule for habits of three or more Loads a day and of more than 60 days' duration, and a 10-day schedule for habits of lesser amounts and duration. To date we have had satisfactory results.

The medical community should be aware that this type of abuse can present in many different ways such as visits for prescriptions, intoxication ranging from ethanollike disinhibition to severe poisoning characterized by deep, cyclical coma or presentation in an emergency room following an accident. Because large amounts of aspirin or acetaminophen (also phenacetin and caffeine in APC preparations) are consumed as part of Loads, a clinician should be alert to possible salicylism, hepatotoxicity or analgesic nephropathy. We have seen patients with salicylate concentrations ranging from 6 to 14 mg per dl in blood specimens drawn two days or more after the last reported Loads ingestion. Glutethimide may also cause hypocalcemia,[6] osteomalacia,[7] peripheral neuropathy and cerebellar impairment,[8] and poor response to chronically prescribed medications (for example, warfarin) as a result of enzyme induction.[9] Determinations of glutethimide concentrations in blood may be helpful in identifying this type of abuse. We recommend that urine be analyzed also because highly tolerant abusers may have nondetectable blood concentrations due to the rapid disappearance of glutethimide from their blood.

The attractiveness of Loads over heroin may be explained by the potent enzyme-inducing property of glutethimide that converts more codeine to morphine than the usual 10 percent after therapeutic analgesic doses.[10] Thus, glutethimide may be able to transform a normally minimally abused narcotic with high side-effect profile and low affinity for the opiate receptor into a potent agonist. Glutethimide also stimulates its own metabolism, and conversion to the more potent and toxic 4-hydroxy-glutethimide may explain the seriousness of overdose and reported fatalities, particularly when combined with ethanol.

We believe that this combination has a potential for widespread abuse. Whether the knowledge of the potentially lethal effects of Loads exerts any curtailment of this spread remains to be seen, and may depend on the continued availability of glutethimide and heroin. The medical community should be aware of the increasing abuse potential of glutethimide. We ourselves have difficulty understanding the continued prescribing of glutethimide as a hypnotic in 1982.

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